UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,757	02/11/2004	Michel Pairet	01-1174-1-C1	3466

28519 7590 11/12/2009

MICHAEL P. MORRIS
BOEHRINGER INGELHEIM USA CORPORATION
900 RIDGEBURY RD
P O BOX 368
RIDGEFIELD, CT 06877-0368

EXAMINER	
BADIO, BARBARA P	

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
11/12/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTO.e-Office.rdg@boehringer-ingelheim.com

Office Action Summary	Application No.	Applicant(s)	
	10/776,757	PAIRET ET AL.	
	Examiner	Art Unit	
	Barbara P. Badio	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,9,10,15-17,19-21,23,25,26,31-37,39 and 63-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,9,10,15-17,19-21,23,25,26,31-37,39 and 63-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

First Office Action on the Merits of a RCE

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 23, 2009 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Application

3. Claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 are pending in the present application and are rejected as indicated below.

Claim Rejections - 35 USC § 112

4. The rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 under 35 USC 112, first paragraph, scope of enablement is withdrawn.

Double Patenting

5. The rejection of claim 1 on the ground of nonstatutory obviousness-type double patenting over claims of copending Application 11/424,244 is withdrawn.

The withdrawal is based on the response to the restriction requirement in the cited copending Application.

Claim Rejections - 35 USC § 103

6. The rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-6 under 35 USC 103 over Nishimura et al. (Allergology International, 1999) and Banholzer et al. (US 5,610,163) in combination is maintained.

Applicant maintains that the combined reference teachings fail to create a prima facie case for obviousness of the claimed invention. Applicant also argues, (a) the declaration of Dr. Bouyssou filed November 4, 2009 shows a surprising and synergistic advantageous benefit in bronchoprotective activity, i.e., evidence of unexpected properties and (b) the cited references do not provide any suggestion to combine the particular steroid and the particular excipients. Applicant's argument was considered but not persuasive for the following reasons.

As noted by applicant, Nishimura shows synergism with a combination comprising oxitropium bromide (an anticholinergic agent) and beclomethasone dipropionate (a corticosteroid) in the treatment of asthma. Thus, the data presented by the Bouyssou's declaration which shows a synergistic effect with the combination of

tiotropium (an anticholinergic agent) and ciclesonide (a corticosteroid) is not unexpected.

Applicant refers to MPEP § 716.02(a)(I) for support that a showing of synergism can be sufficient proof of nonobviousness. However, MPEP § 716.02(a)(I) states:

> Evidence of a greater than expected result may also be shown by demonstrating an effect which is greater than the sum of each of the effects taken separately (i.e., demonstrating "synergism"). *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989). However, a greater than additive effect is not necessarily sufficient to overcome a *prima facie* case of obviousness because such an effect can either be expected or unexpected. Applicants must further show that the results were greater than those which would have been expected from the prior art to an unobvious extent, and that the results are of a significant, practical advantage. *Ex parte The NutraSweet Co.*, 19 USPQ2d 1586 (Bd. Pat. App. & Inter. 1991) (Evidence showing greater than additive sweetness resulting from the claimed mixture of saccharin and L-aspartyl-L-phenylalanine was not sufficient to outweigh the evidence of obviousness because the teachings of the prior art lead to a general expectation of greater than additive sweetening effects when using mixtures of synthetic sweeteners.).

According to MPEP § 716.02(a)(I), a greater than additive effect is not necessarily sufficient to overcome a prima facie case of obviousness because such can either be expected or unexpected. It is the examiner's position that the showing of the Bouyssou's declaration is not unexpected since as noted by applicant, Nishimura provides a showing of synergism of a combination an anticholinergic agent and a corticosteroid. Also as noted by the MPEP, applicant "must further show that the results were greater than those which would have been expected from the prior art to an obvious extent, and that the results are of a significant, practical advantage". Applicant

has not shown that the synergism shown in the Bouyssou's declaration is greater than one of skilled in the art would expect based on the teachings of Nishimura.

In response to the argument that the prior art does not provide any suggestion to combine the particular steroid and the particular excipient(s), the examiner notes that Nishimura teaches the combination of an anticholinergic agent and a corticosteroid and the synergism of said combination in the treatment of asthma. Ciclesonide is a known corticosteroid, thus its use in the composition of Nishimura would be obvious to the skilled artisan. Banholzer teaches esters of thienyl carboxylic acids such as tiotropium as anticholinergic agents with **prolonged activity** useful in treating asthma. The prolonged activity as Banholzer would provide the motivation to modify the combination of Nishimura by replacing the anticholinergic agent, oxitropium bromide with a thienyl ester such as tiotropium as taught by Banholzer. The composition of the two active ingredients with a pharmaceutically acceptable excipients as recited by the instant invention is also prima facie obvious based on the level of skill of the ordinary artisan in the art as it relates to the production of inhalable powders.

In summary, the cited prior art makes obvious the synergism of a composition comprising an anticholinergic agent and a corticosteroid. The prior art teaches (a) the claimed tiotropium as an anticholinergic agent having prolonged therapeutic activity in the treatment of asthma and (b) the claimed ciclesonide as a corticosteroid useful in treating asthma. Based on teaching of the prior art, the claimed artisan would have the reasonable expectation that the combination of tiotropium and ciclesonide would also have a synergistic effect in the treatment of asthma.

For these reasons and those given in the previous Office Action, the rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-6 under 35 USC 103 over Nishimura et al. (Allergology International, 1999) and Banholzer et al. (US 5,610,163) in combination is maintained.

7. The rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-6 under 35 USC 103 over Keller et al. (WO 00/28979, see English equivalent US 6,645,466), Nishimura et al. (Allergology International, 1999) and Banholzer et al. (US 5,610,163) in combination is maintained.

In addition to the argument discussed above in #6, applicant argues Keller does not make up for the deficiencies of the Nishimura and Banholzer references because Keller does not provide a suggestion to specifically combine tiotropium, ciclesonide and one of the specific excipients as recited by the instant claims. Applicant also argues Keller provides no hint that such a combination would provide unexpected synergistically advantageous properties. Applicant's argument was considered but not persuasive for the following reasons.

The examiner's response to the argument against Nishimura and Banholzer are as discussed above in #6. The examiner maintains that the claimed composition is obvious based on the teaching of the prior art and the level of skill of the ordinary artisan in the art at the time of the present invention.

Keller was utilized in combination with Nishimura and Banholzer for its teaching of (a) inhalable powder formulation including those comprising a beta-mimetic and/or an

anticholinergic agent and/or a corticosteroid (said combination would encompass the claimed composition), (b) carriers such as glucose, lactose, sucrose, etc., (c) tiotropium bromide and ciclesonide as an anticholinergic agent and a corticosteroid, respectively and (d) particle size of approximately 10 to 500 µg as discussed in the previous Office Action. Nishimura provides the motivation to combine an anticholinergic agent and a corticosteroid based on the teaching of synergism and Banholzer provides the motivation to utilize tiotropium based on the teaching of prolonged anticholinergic activity. Keller provides the teaching of dry powder inhalable formulations and the use of the specific excipients as recited by the instant claims.

For these reasons and those given in the previous Office Action, the rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-6 under 35 USC 103 over Keller et al. (WO 00/28979, see English equivalent US 6,645,466), Nishimura et al. (Allergology International, 1999) and Banholzer et al. (US 5,610,163) in combination is maintained.

Telephone Inquiry

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Barbara P. Badio/
Primary Examiner, Art Unit 1628